Research Article

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Efficacy of Platelet Rich Plasma in Third Molar Impaction Surgery: A Prospective Randomized Control Study

Joy R Das[1] Ajoy Vijayan[2*] Arjun Gopinath[3] Mahesh B Pillai[4]

[1]Associate Professor, Department of Oral and Maxillofacial Surgery, Mahe Institute of Dental Sciences, Mahe, Pondicherry, India.
[2]Professor and Head, Department of Oral and Maxillofacial Surgery, Mahe Institute of Dental Sciences, Mahe, Pondicherry, India.
[3]Associate Professor, Department of Oral and Maxillofacial Surgery, Kannur Dental College, Anjarakkandy, Kannur, India.
[4]Associate Professor, Department of Prosthodontics, Noorul Islam College of Dentistry, Trivandrum, Kerela, India.

ABSTRACT

Background: The use of autologous platelet concentrates mainly platelet rich plasma has been of relevance recently in the field of Oral and Maxillofacial surgery. These concentrates had the ability to improve the hard and soft tissue healing. This ability of the platelet concentrates had been studied in the healing after mandibular third molar impaction surgery. The various parameters like bone density and post operative pain, were taken into account. The patients were evaluated on 1st,2nd.7th day, first month and second month post operatively. The values for each parameters were found out and tabulated. Platelet-rich fibrin (PRF) is a fibrin meshwork, in which platelet cytokines, growth factors, and cells are entrapped and discharged after a period and can serve as a resorbable film. PRF is the next generation of platelet concentrates equipped to improve arrangement without biochemical blood handling.

Materials and methods: Twelve patients, seven males and five females with bilaterally impacted mandibular third molars were included in the study. Autologous platelets were concentrated. This was applied on one of the sockets which was randomly taken as the test side. The other socket was treated as the control.

Results: Statistical analysis was done using Mann Whitney U test for pain which revealed the values for pain being statistically significant for the test side. Bone density was analysed with T-test . Bone density values were statistically significant for the test side.

Summary and conclusion: platelet rich plasma is a surgical additive that can be used to improve bone and soft tissue healing. It contains a wide array of growth factors that are responsible for their healing potential.

Keywords: Platelet concentrates, growth factors, bone density, gray value scale, pain, platelet rich fibrin.

INTRODUCTION

A lot of surgical additives have been introduced into the field of Oral and Maxillofacial Surgery with the aim of better soft and hard tissue healing and prevention of postoperative complications. Fibrin adhesives or fibrin glue were the first ones to be used as platelet concentrates for tissue healing. The evolution of platelet concentrates, thus dates back to 1970 when fibrin glue was introduced. This product was available in blood bank and this carried a risk of disease transmission, like hepatitis and HIV, thereby leading to its ban in 1977.[1] After this studies were concentrated on the preparation of autologous platelet concentrates .This was introduced into the field of Oral and Maxillofacial Surgery in 1998,by Marx.

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*Correspondence Dr. Joy R Das.
Department of Oral and Maxillofacial Surgery, Mahe Institute of Dental Sciences, Mahe, Pondicherry, India.
Email: drjoy303@gmail.com

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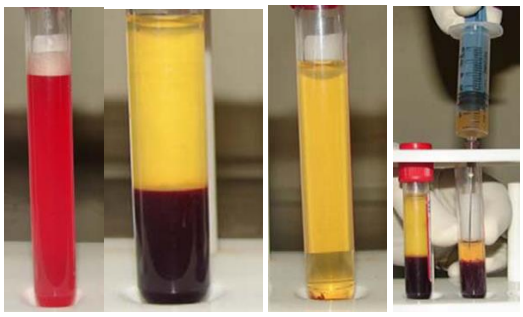

Fig 1 to 4: Centrifugation and PRF obtained.

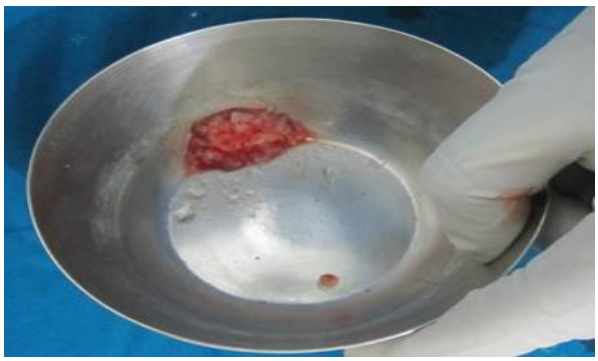

Fig 5: PRF mixed with hydrogel.

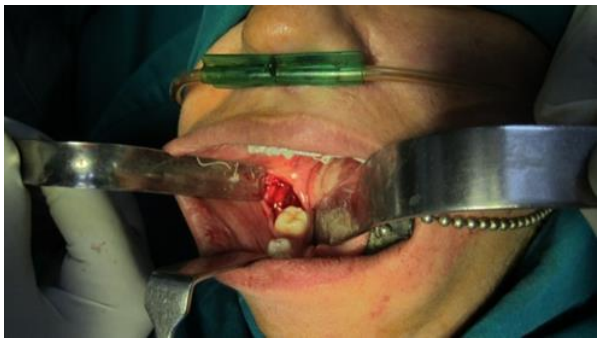

Fig 6: PRF placement.

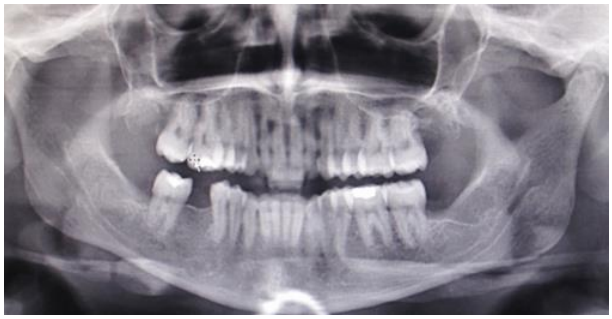

Fig 7: OPG after 1 month duration.

The various uses of platelet rich plasma in Oral and maxillofacial surgery includes sinus lift procedures, ridge augmentations, socket preservation,impaction and open extractions requiring some amount of

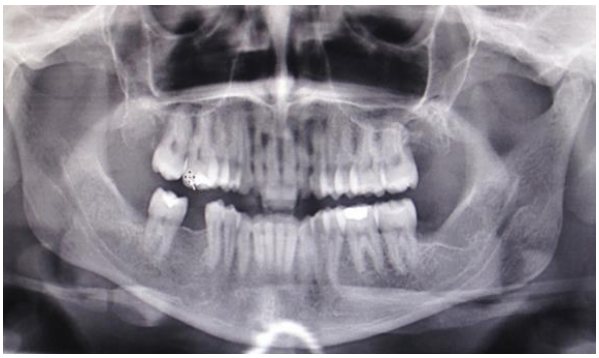

Fig 8: OPG after 2 month duration

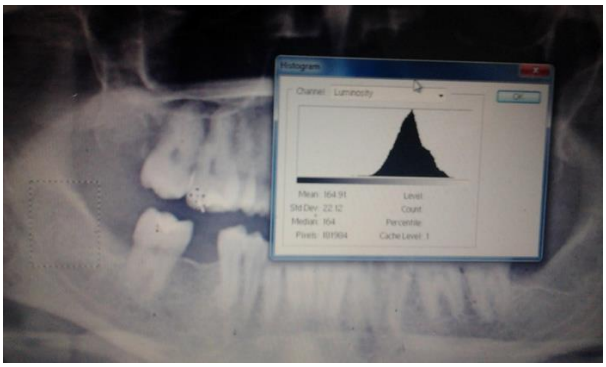

Fig 9: Comparison of the gray scale value using adobe photoshop.

bone guttering, alveolar cleft and palate repair, alveolar bone grafting, oral or nasal fistula closure, intrabony defects, jaw reconstruction , mandibular fractures , and soft tissue gingival procedures.[4]

The growth factors present in the platelet concentrates initiate connective tissue healing, bone regeneration and repair, increase mitogenesis of fibroblasts, stimulates angiogenesis in the wound bed and activates macrophages. The newly created blood vessels and blood flow brings necessary nutrients and oxygen for optimal healing. The growth factors act on stem cells , osteoblast precursors and fibroblasts.[5] The current study deals with the efficacy of autologous platelet concentrates in third molar impaction surgery.

MATERIALS AND METHODS

This prospective, randomized double blinded control trial was conducted in Kannur Dental College, Kannur District, Kerala ,India .This study protocol was approved by the Institutional Review Board and Ethical Committee. Informed consent was obtained from all patients. Healthy non diabetic individuals between 18 and 34 years of age

with bilaterally impacted mandibular 3rd molars were selected. Those on recent antibiotics or steroid use,systemic immunodeficiency ,chemotherapy and radiation therapy and any other immunocompromise were excluded from the study. The patients selected were enrolled for the study and preoperative Intra Oral Periapical Radiographs and Orthopantomograms were taken. Twelve patients, 7 males and 5 females, who presented with bilaterally impacted mandibular molars and in similar positions were selected. All patients underwent bilateral surgical removal of impacted 3rd molars. The two operated sides in each patient were randomly divided into two study groups: test and control. Extraction of the impacted mandibular third molar at one side whose socket was simply sutured was called the control side, while the opposite impacted third molar socket, which was filled with PRP gel and sutured was called the test side. The sockets where PRP is to be placed were randomly selected. Patients were recalled on first, second day,third day, first week, fourth week and two months postoperatively, for follow up study.

Preparation of PRP gel was done in the following way. Blood is drawn intravenously from the anticubital region of patients forearm using vacutainer needle and vacutainers containing Citrate Phosphate Dextrose Anticoagulant (CPDA, 0.8ml each). This anticoagulant is preferred because it preserves the platelet membrane integrity. The Vacutainers were thoroughly shaken to ensure maximum mixing of the anticoagulant with the drawn blood. The anticoagulant avoids platelet degranulation and activation. In first centrifugation the whole blood is centrifuged at 2400 r.p.m. for 10 mins. It is called as soft spin which allows blood separation into three layers . The layers are bottom most layer (RBC 55% of total volume), top most acellular plasma (40% of total volume) and intermediate layer (5% of total volume) which is called as buffy coat layer. The platelet poor plasma, platelet rich plasma and some RBCs are transferred into another tube without anticoagulant. (Fig 1,2,3,4)

This tube will now undergo second centrifugation at 3600 rpm for 10 minutes which is faster than the first. This is called as the hard spin. This allows the platelet to settle at the bottom of the tube with very little RBC, which explains the red tinge of the PRP preparation. The acellular PPP (80 % of the total volume) is found at the top. Most of this platelet poor plasma is removed with the syringe and is discarded and the remaining PRP is shaken well and mixed with hydrogel(Fig 5)

All the cases were done under conscious sedation with intravenous Midazolam upto 5 mg with monitoring of blood pressure and oxygen saturation using a multiparameter. Inferior alveolar nerve block, lingual nerve block and long buccal nerveblock were administered using 2% lignocaine hydrochloride with 1: 2,00,000 adrenaline, standard Ward's incision was followed in all the cases. Full thickness mucoperiosteal flap was raised to expose sufficient bone on lateral and distal aspect of the impacted molar. Removal of bone was done with 702 carbide bur.

Constant irrigation was done with normal saline while removing bone to prevent thermal necrosis. Surgical removal of impacted tooth was done. The surrounding bone was smoothened. The wound was gently irrigated with sterile saline solution and checked for any small detached fragments of bone or tooth pieces. Surgical removal of impacted mandibular 3rd molar was done on the opposite side in the similar way and one of the extraction socket was randomly chosen by the operator. The pre processed PRP was taken into the sterile stainless steel bowl and 0.5ml of $CaCl_2$ was mixed to obtain the PRP gel, which was placed into the selected extraction socket and primary closure of the wound was done .No graft material was added to PRP in this study. Wound was closed with a 3-0 black braided silk interrupted suture.(Fig 6)

Pain was measured using visual analogue scale (VAS).[6] A 10-point visual analog scale (VAS) with a score of 0 indicating "no pain" and 10 indicating "very severe pain" was used to assess pain on post operative days one , three and seven.

Radiographic evaluation for bone density Orthopantomograms were taken preoperatively,at the second and eighth week respectively to assess and compare radiographic bone densities between PRP and non PRP sites. The radiographic bone densities were evaluated by Adobe Photoshop Software.[9] The bone densities could be measured at the alveolar crest levels, furcation level and the apical region of the surgically removed mandibular

Table 1: Assessment of pain following VAS.

Days	First day		Third day		Seventh day	
Sl no	Test	Control	Test	Control	Test	Control
1	3	4	2	2	0	2
2	3	4	2	4	1	1
3	4	3	3	4	0	0
4	3	5	2	4	1	1
5	2	5	2	3	0	0
6	2	6	1	4	0	2
7	3	4	2	3	1	2
8	4	3	4	2	1	0
9	3	3	3	2	1	1
10	3	5	2	4	1	1
11	3	4	2	2	0	0
12	2	4	3	2	1	1

Table 2: Mann Whitney U Test for pain.

Test statistics	Pain score (day 1)	Pain score (day 3)	Pain score (day 7)
Mann Whitney U	21.500	45.000	55.500
Asymp. Significance (2 tailed)	0.002	0.091	0.293

Mean and Standard deviation

Table 3: Descriptive statistics.

	N	mean	Std. deviation	mininum	maximum
Day 1	24	3.5417	1.0206	2.00	6.00
Day 3	24	2.6667	0.916	1.00	4.00
Day 7	24	0.7500	0.675	0	2.00
category	24	0.50	0.511	0	1

Table 4: Mann Whitney U test for soft tissue healing assessment.

	N	Mean	Std. Deviation	minimum	maximum
Day 1	24	3.0417	0.69025	2.00	4.00
Day 3	24	3.8333	0.63702	2.00	5.00
Day 7	24	4.6667	0.48154	4.00	5.00
category	24	0.50	0.511	0	1

Table 4b: Descriptive statistics.

	N	Mean	Std. Deviation	minimum	maximum
Day 1	24	3.0417	0.69025	2.00	4.00
Day 3	24	3.8333	0.63702	2.00	5.00
Day 7	24	4.6667	0.48154	4.00	5.00
category	24	0.50	0.511	0	1

Table 5: Gray value scale at one month.

Sl no	Test	Control
1	164	141
2	159	132
3	118	98
4	126	120
5	151	143
6	116	130
7	123	116
8	138	112
9	141	130
10	150	141
11	159	141
12	143	132

Table 6: Gray value scale at two month.

Sl no	Test	Control
1	166	147
2	161	138
3	133	108
4	128	124
5	159	147
6	126	133
7	133	129
8	139	131
9	144	131
10	151	139
11	162	143
12	145	133

Table 7: Paired T test for bone density.

	t	difference	Significance
Grey value at first month	2.032	22	0.054
Grey value at second month	2.341	22	0.029

third molars. In the present study the apical region of the removed molars were taken to measure the bone densities.

Orthopantomogramic images were digitalized using the Sidexis software. The image was transferred to Adobe Photoshop.The grey scale values were measured. The grey scale values were compared at the PRP and non PRP sides in the same OPG.(Fig 7,8,9) The statistical analysis done was Mann Whitney U test for pain and soft tissue healing while the analysis used for bone density and swelling was a paired T test.

RESULTS

Assessment of pain by visual analogue scale on first post operative day showed mean pain score of 2.91 at the test site and 4.16 at the control site (P value – 0.002). On the third day the mean score on the test site was 2.33 while that on the control site was 2.91 (P value 0.091). On the seventh post operative day the mean on the test site was 0.58 while on the control side was 0.91.(P value 0.293). (Table1,2,3,4)

Assessment of gray value scale was done using the Adobe Photoshop software. The mean value obtained for the gray value scale for the control side was 140.91 and for the test side was 128.63 (P value 0.054) at the end of one month. The mean value of the gray scale obtained at the end of the second month was 145.58 for the control side and 133.58 for the test side (P value 0.029). The values btained for the bone density for the control and the test side showed that PRP created a statistically significant difference.(Table 5,6,7)

DISCUSSION

PRP can be defined as a volume of autologous plasma that has a platelet concentration above the base line. Normal platelet count in blood ranges from 1,50,000 to 4,00,000 / µL. Since the scientific proof of bone and tissue healing has been shown using PRP with 10,00,000 platelets / µL it is this concentration of platelets in a 5 mL volume of plasma.[5,6,7,8] Since PRP is developed from autologous plasma, it is inherently safe and free from transmissible diseases like HIV and hepatitis . Within PRP the increased number of platelets delivers an increased number of growth factors to surgical area.

Growth factors are:Platelet Derived Growth Factor (alpha and beta), Tissue Growth Factor, Vascular Endothelial Growth Factor, Epidermal Growth Factor , Connective Tissue Growth Factor, Fibroblast Growth Factor, Keratinocyte Growth Factor ,G/MCSF- Granulocyte/Macrophage Colony Stimulating Factor, Tumour Necrosis Factor. [9,10,11] Thus PRP is a combination of 7 growth factors with the normal clot as carrier. The clot is composed of fibronectin, fibrin and vitronectin which are cell adhesion molecules required for cell migration as well as in osteoconduction , wound epithelialization and osseointegration.[12]

PRP acts on fibroblasts to increase their number (mitogenesis) and stimulate vascular ingrowth (angiogenesis). PRP is best developed from autogenous whole blood shortly or at the beginning of surgical procedure. Once developed, PRP is stable and remains sterile in the anticoagulated state for 8 hours. Platelet concentrates may contain small amounts of leukocyte that synthesise interleukins, involved in the non specific immune reaction. In the recent years several regenerative procedures such as grafting the socket with autologous bone or bone substitutes along with platelet concentrates have been developed.[13]

Orthopantomograms revealed that the effects of PRP were significantly beneficial for increasing bone density following surgery. The increase in bone density suggests a greater volume of new bone formation with PRP treatment. Moreover, the increase in bone density (presumed as increased volume of new bone formation) was found to occur at earlier time points than non-PRP treated control sites. This corresponds with results from molecular studies that demonstrated PRP treatment of human mesenchymal stem cells induced ,early proliferation of these cells and possibly differentiation into osteoblasts.

Soft tissue wound healing and bone growth involve physiologic cascades in which cellular and hormonal factors play pivotal roles. The rationale for applying platelet gel is based on the delivery of platelet growth factors to tissues and on the fact that platelet α-granules, found inside the platelets,

contain a variety of growth factors . Platelet gel growth factors are peptides that promote cell proliferation, differentiation, chemotaxis, and the migration of various cells involved in wound healing.[14]

The visual analogue scale clearly indicates the reduction of pain in the test group in this study. The pain on the first and third day was comparatively less in the PRP side than the non PRP side. There has not been a valid reason why the pain is less in the PRP side. But there has been many studies indicating that the application of PRP gel substantially reduced the pain postoperatively.

The second generation platelet rich fibrin (PRF) was first developed in France by Choukroun for specific use in oral and maxillofacial surgery.[15]This technique requires neither anticoagulant nor bovine thrombin (nor any other gelling agent), which is considered to be more advantageous than PRP these days because of the simplicity in its preparation.

PRF membrane protects the surgical site and promotes soft tissue healing. It acts as a biological connector between different graft elements and as a matrix that supports neoangiogenesis, capturing stem cells and migration of osteoprogenitor cells to the center of the graft. Currently, PRF seems to be an accepted minimally invasive technique with minimal risks and good clinical results

To conclude, from the study conducted we have come to a conclusion that platelet rich plasma has beneficial effects on the improvement of bone density and reduction of pain after mandibular third molar impaction surgery.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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